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(54) Title: PHARMACEUTICALLY ACTIVE 4-SUBSTITUTED PYRIMIDINE DERIVATIVES

(57) Abstract: The present invention relates to the use of certain 4-substituted pyrimidine derivatives as mGluR1 antagonists, to novel 4-substituted pyrimidine derivatives, to pharmaceutical formulations comprising 4-substituted pyrimidine derivatives, to a process for preparing 4-substituted pyrimidine derivatives and to intermediates useful in the preparation of 4-substituted pyrimidine derivatives.

INTERNATIONAL SEARCH REPORT

Intern. Application No

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D239/94 C07D239/95 C07D471/04 C07D491/04 C07D495/04
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 607 439 A (EISAI) 27 July 1994 (1994-07-27) page 1 -page 13; claims; table ALL	1,2,4,11
A	EP 0 566 226 A (ZENECA) 20 October 1993 (1993-10-20) page 1 -page 20; claims	1
X	claims; examples 1-80	11,25,26
A	WO 97 49689 A (PHARMACIA & UPJOHN) 31 December 1997 (1997-12-31) page 1 -page 26	1
X	page 27 -page 44; claims 1,12,16	11,23, 25,26

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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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Date of the actual completion of the international search

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 414 386 A (LILLY) 27 February 1991 (1991-02-27) claims 1,7,9	1
X	claims; examples 1-100	11,12, 23,25,26
A	FR 2 393 531 A (SANKYO) 5 January 1979 (1979-01-05) claims	1
X	page 1 -page 34	11,12, 25,26
P,X	DE 199 04 710 A (AVENTIS) 10 August 2000 (2000-08-10) page 1 -page 18	1,11,25, 26

INTERNATIONAL SEARCH REPORT

Intern. Application No

PCT/US 00/26261

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 607439 A	27-07-1994	AU 668363 B	02-05-1996
		AU 2685192 A	03-05-1993
		FI 941417 A	25-03-1994
		KR 138695 B	01-10-1998
		NO 941101 A	30-05-1994
		US 5576322 A	19-11-1996
		CA 2116336 A	15-04-1993
		CN 1071164 A	21-04-1993
		HU 70854 A	28-11-1995
		WO 9307124 A	15-04-1993
		JP 3081172 B	28-08-2000
		JP 10095776 A	14-04-1998
		JP 2818487 B	30-10-1998
		JP 2000264877 A	26-09-2000
		JP 2000273089 A	03-10-2000
		JP 2000264885 A	26-09-2000
		MX 9205542 A	31-03-1993
		NZ 244526 A	26-07-1995
		PT 100905 A	28-02-1994
		US 5693652 A	02-12-1997
		US 5801180 A	01-09-1998
		ZA 9207465 A	13-04-1993
EP 566226 A	20-10-1993	AT 130000 T	15-11-1995
		AU 661533 B	27-07-1995
		AU 3101093 A	22-07-1993
		CA 2086968 A,C	21-07-1993
		CZ 282038 B	16-04-1997
		DE 69300754 D	14-12-1995
		DE 69300754 T	28-03-1996
		DK 566226 T	18-03-1996
		ES 2078798 T	16-12-1995
		FI 930208 A	21-07-1993
		GR 3018143 T	29-02-1996
		HK 36497 A	04-04-1997
		HU 63153 A	28-07-1993
		HU 9500185 A	28-07-1995
		IL 104479 A	22-12-1999
		KR 229294 B	01-11-1999
		MX 9300277 A	30-06-1994
		NO 301541 B	10-11-1997
		NZ 245662 A	26-09-1995
		RU 2127263 C	10-03-1999
		SK 1693 A	09-09-1993
WO 9749689 A	31-12-1997	US 5457105 A	10-10-1995
		US 5616582 A	01-04-1997
		ZA 9300015 A	20-07-1993
		JP 2994165 B	27-12-1999
		JP 6073025 A	15-03-1994
		AU 3094197 A	14-01-1998
		BR 9702328 A	20-07-1999
		CA 2228492 A	31-12-1997
		CN 1198158 A	04-11-1998
		EP 0853616 A	22-07-1998
		HU 9902026 A	28-04-2000
		JP 11511761 T	12-10-1999
		NO 980718 A	08-04-1998

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/26261

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9749689 A		PL 325122 A	06-07-1998
		US 6057326 A	02-05-2000
EP 414386 A	27-02-1991	US 5034393 A	23-07-1991
		AU 634562 B	25-02-1993
		AU 5982690 A	31-01-1991
		BR 9003634 A	27-08-1991
		CA 2021925 A	28-01-1991
		JP 3066689 A	22-03-1991
		US 5350749 A	27-09-1994
FR 2393531 A	05-01-1979	JP 1355582 C	24-12-1986
		JP 54017123 A	08-02-1979
		JP 61020522 B	22-05-1986
		BR 7803642 A	09-01-1979
		CA 1086642 A	30-09-1980
		CA 1230339 B	15-12-1987
		CH 636751 A	30-06-1983
		DE 2824768 A	14-12-1978
		GB 1598880 A	23-09-1981
		GB 1582407 A	07-01-1981
		NL 7806153 A,B,	11-12-1978
		PH 13938 A	04-11-1980
		SU 1111675 A	30-08-1984
		US 4323680 A	06-04-1982
		US 4213987 A	22-07-1980
		ZA 7803229 A	27-06-1979
DE 19904710 A	10-08-2000	AU 2292900 A	25-08-2000
		WO 0046214 A	10-08-2000

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